Histological and functional benefit following transplantation of motor neuron progenitors to the injured rat spinal cord.

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Public Summary:

Scientific Abstract:
BACKGROUND: Motor neuron loss is characteristic of cervical spinal cord injury (SCI) and contributes to functional deficit. METHODOLOGY/PRINCIPAL FINDINGS: In order to investigate the amenability of the injured adult spinal cord to motor neuron differentiation, we transplanted spinal cord injured animals with a high purity population of human motor neuron progenitors (hMNP) derived from human embryonic stem cells (hESCs). In vitro, hMNPs displayed characteristic motor neuron-specific markers, a typical electrophysiological profile, functionally innervated human or rodent muscle, and secreted physiologically active growth factors that caused neurite branching and neuronal survival. hMNP transplantation into cervical SCI sites in adult rats resulted in suppression of intracellular signaling pathways associated with SCI pathogenesis, which correlated with greater endogenous neuronal survival and neurite branching. These neurotrophic effects were accompanied by significantly enhanced performance on all parameters of the balance beam task, as compared to controls. Interestingly, hMNP transplantation resulted in survival, differentiation, and site-specific integration of hMNPs distal to the SCI site within ventral horns, but hMNPs near the SCI site reverted to a neuronal progenitor state, suggesting an environmental deficiency for neuronal maturation associated with SCI. CONCLUSIONS/SIGNIFICANCE: These findings underscore the barriers imposed on neuronal differentiation of transplanted cells by the gliogenic nature of the injured spinal cord, and the physiological relevance of transplant-derived neurotrophic support to functional recovery.